

## Remarks

After amendment, claims 40-66 are now pending in the present application, numerous claims having been cancelled pursuant to the Examiner's restriction requirement and Applicants' election of claims to prosecute. Support for the amendment to the claims can be found throughout the originally filed application and claims. All subject matter in the newly presented claims can be found in the originally filed claims. No new matter has been added by way of this amendment.

Applicants note that any subject matter which is cancelled herein, including any subject matter canceled from the original claims is made *without prejudice* in order to give Applicant a chance to consider filing any one or more divisional/continuation applications to seek allowance of that subject matter. The present amendments have been made to expedite allowance of the instant application.

### *Rejections*

The Examiner has rejected the originally filed claims variously under the judicially created doctrine of obviousness-type double patenting, as well as 35 U.S.C. §112, second paragraph, §102(b) and §103 for the reasons which are stated in the Examiner's office action of August 26, 2008. Applicant shall address each of the Examiner's objections/rejections in the sections which follow.

### The Obviousness-type Double Patenting Rejection

The Examiner has rejected previously pending claims 1, 2, 5 and 7 on the ground of nonstatutory obvious-type double patenting over claims 1 and 9-10 of U.S. patent no. 6,369,078. The claims of the '078 patent are directed to method claims (only methods are claimed) which relate to a method for reducing, preventing or repelling the spread of a colony or population of fire ants. It is respectfully submitting that the methods of the '078 patent clearly do not render *any* of the originally filed claims of the present

invention obvious. Those claims do not suggest the originally claimed pharmaceutical compositions (i.e., compositions which are administered to patients for the treatment of tumors or cancer) or the originally claimed methods. Notwithstanding the obvious lack of relevance of the claims of the '078 patent to those of the originally presented claims, Applicants note that the originally filed pharmaceutical composition claims have been cancelled, thus rendering this rejection moot in any event. The Examiner is respectfully requested to withdraw this rejection.

#### The §112, Second Paragraph Rejection

The Examiner has rejected originally filed claim 15 under 35 U.S.C. §112, second paragraph as being indefinite. In particular, the Examiner questions the use of the term "lymphangiogenesis" in claim 15 which is directed to a method of treating a tumor or cancer. Inasmuch as lymphangiogenesis is not a tumor or cancer but is an angiogenesis condition for which appropriate therapy according to the present invention may be provided, but which invention was not elected to be prosecuted pursuant to the Examiner's restriction requirement, Applicants have presented method treatment claims in this application which do not incorporate this term. It is noted that Applicants reserve the right to file one or divisional applications related to the treatment of angiogenesis, and in particular, lymphangiogenesis.

It is respectfully submitted that the presently claimed invention meets the requirements of 35 U.S.C. §112, second paragraph.

#### The §102 Rejections

##### *Based Upon Rehmert, the '209 Patent*

The Examiner has rejected previously submitted claims 1-2, 5 and 7 as being anticipated by Rehmert, US patent no. 4,910,209 (Rehmert) for the reasons which are stated in the office action on pages 4-5. It is the Examiner's contention that Rehmert

disclosed certain compositions which were originally claimed having one or more compounds which were to be included therein. Applicants have cancelled the claims which are directed to pharmaceutical compositions *without prejudice* to advance prosecution of the instant application, thus rendering this rejection moot. Applicants note that they have specifically reserved the right to refile claims directed to pharmaceutical compositions in subsequent applications.

Separately, the Examiner has rejected previously filed claims 1, 8 and 15 as being anticipated by Goulet, al., US patent no. 5,849,764 (Goulet) for the reasons which are stated in the office action on page 5. It is the Examiner's contention that Goulet anticipates claims 1, 8 and 15 inasmuch as Goulet discloses certain piperidine derivatives (see column 86) and also teaches that the compounds may be used to treat breast cancer. Consequently, the Examiner maintains that Goulet anticipates the present invention. Applicants respectfully traverse the Examiner's rejection.

Inasmuch as claims 1 and 8 have been cancelled from the instant application *without prejudice*, any further discussion of the impact of the disclosure of Goulet on originally filed claims 1 and 8 have been rendered moot. Regarding the impact of the disclosure of Goulet on original claim 15, Applicants respectfully submit Goulet does not anticipate originally filed claim 15, subject matter of which is now presented in a number of the newly presented claims.

The present invention is directed to numerous *trans-1,6-disubstituted* piperidine compounds which have shown significant activity against tumors and cancers as a consequence of anti-angiogenesis activity. While numerous substituents are claimed within the generic chemical structures otherwise presented, it is noted that these compounds are all *trans-disubstituted* piperidines. The Goulet reference discloses literally *millions*, if not *billions* of compounds, two of which (13JJ and 13KK in column 85-86) have piperidine moieties. The compounds which Goulet discloses do not anticipate the present invention inasmuch as the Goulet compounds are substituted aryl-substituted indole compounds having a complex structure which appears at lines 18-25 of

column 80. Of the complex structures which are disclosed by Goulet, compounds 13JJ and 13KK indicate the two general substituents which are found on the complex aryl-substituted indole structure which is presented in column 80 of Goulet. Each of these substituents is itself quite complex. It is noted that the compounds of Goulet are not even remotely related to compounds which are claimed in the method aspects of the present invention, given that the presently claimed chemical structures and the definitions which are provided in the specification for the term “substituents”, which may be found on the groups otherwise claimed, clearly and unequivocally distinguishes over any arguable relationship which one might posit to exist between Goulet and the compounds used in the present invention.

Notwithstanding those obvious, gross differences between the compounds which are used in the present invention and the compounds which are disclosed by Goulet, it is noted that Goulet does not even specify the trans-configuration in compounds 13JJ and 13KK (regardless of how unrelated compounds 13JJ and 13KK are to the present invention), thus further eliminating Goulet as an anticipated reference. There is simply no way to cogently argue that Goulet anticipates the present invention. It is respectfully requested that the Examiner withdraw his rejection that the claims are anticipated by Goulet.

#### The §103 Rejection

The Examiner has rejected previously pending claim 1, 8, 15 and 38-39 as being obvious over Goulet in view of Falk, et al., US patent no. 6,147,059 (Falk) for the reasons which are set forth in the specification on page 6. The Examiner cites Goulet for the disclosure of compositions which are claimed in the present invention and cites Falk generically, for teaching that a composition which treats basal cell cancer by delivering drugs such as hyaluronic acid (see column 1, lines 18-35 of Falk). Applicants respectfully traverse the Examiner's rejection.

As set forth in the claims of the present application, the present invention relates to the use of certain trans-disubstituted piperidine compounds to treat a number of tumors and cancer as otherwise claimed. The disubstituted piperidine analogs as claimed exhibit anti-angiogenesis properties which provides activity to treat tumors and cancer according to the present invention. Contrary to the Examiner's contention, neither Goulet nor Falk teaches or suggests the present invention.

Goulet, described above, is directed to a large of compounds which have an aryl-substituted indole pharmacophore which are said to be useful to treat a variety of sex hormone related and other conditions in men and women. Goulet does not disclose any of the compounds of the present invention and there is simply no way that one of ordinary skill could possibly appreciate the activity of compounds which are used in the present invention. As discussed above, Goulet literally discloses millions, if not billions of compounds, the closest of which are compounds 13JJ and 13KK which appear in column 86 of Goulet. But as described in great detail hereinabove, those compounds are unrelated to the present invention and describe compounds which are infinitely more complex than those of the present invention. In addition, nowhere in Goulet is there even a remote teaching or oblique suggestion of trans-disubstituted piperidines which form the basis of the present application. To suggest that one of ordinary skill will take compounds 13JJ and 13KK of Goulet, strip off all of the chemical complexity which forms the basis of the Goulet teachings, and further impose stereochemically situated substituents, which are clearly distinguishable from those used by Goulet to come up with the present invention is simply not cogent. It is quite the Goulet neither teachings nor discloses the presently claimed invention.

Turning to the disclosure of Falk, Falk generally teaches the use of non-steroidal anti-inflammatory drugs in combination with hyaluronic acid for the treatment of or to resolve a disease or tissue of the skin, one of which may be cutaneous malignancies such as are treated by the present invention. There is absolutely no disclosure or suggestion of trans-disubstituted piperidine compounds which are used in the present invention and

certainly there are no teachings or suggestions whatsoever in Falk which might be taken to somehow obviate the deficiencies of Goulet and lead the person of ordinary skill to the present invention.

Applicants submit that the teachings of Goulet, in view of Falk, can in no way be taken to suggest the present invention or render the present invention unpatentable. It is axiomatic that a reference (Goulet) which does not teach or even remotely suggest the compounds of the present invention cannot be combined with another reference, in this case Falk, which also completely fails to mention the presently claimed compounds or their use in treating cutaneous malignancies, to provide the present invention. To cogently argue that a reference is rendered obvious by a combination of disclosures, the disclosures of each reference must at least point to the individual features of the rejected invention. Here, the Examiner has cited Goulet, which, as described in great detail hereinabove, does not disclose or even remotely suggest compounds according to the present invention, with the Falk disclosure, which is even further removed from any chemical structural relevance. The combined references of Goulet and Falk simply do not make out a credible obviousness rejection.

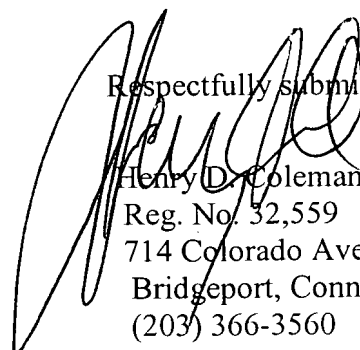
In short, it is respectfully submitted that the combination of references cited by the Examiner does not cogently support an argument that the present invention is unpatentable. Consequently, Applicants respectfully submit that the present invention is non-obvious over the cited references.

For all of the reasons which are set forth hereinabove, Applicants respectfully submit that the application is in condition for allowance and early action resulting in allowance of the instant application is earnestly solicited.



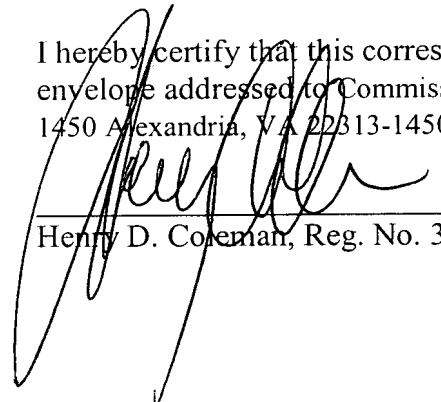
A fee for the presentation of seven (7) dependent claims is enclosed (\$182). A petition for a two month extension of time is enclosed as is the appropriate fee. Please charge any fee due or credit any overpayment previously made to Deposit Account No. 04-0838.

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Respectfully submitted,  
  
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#### Certificate of Mailing

I hereby certify that this correspondence is being sent by First Class Mail in an envelope addressed to Commissioner for Patents, Mail Stop Amendment, P.O. Box 1450 Alexandria, VA 22313-1450 on January 26, 2009.

  
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